Remarks

I. Status of the Claims and Support for Amendments

The Non-Final Office Action dated August 10, 2007 has been carefully reviewed and the following reply is made in response. Reconsideration of this Application is respectfully requested. All previously pending claims have been canceled without prejudice and without disclaimer of the subject matter therein. Applicants reserve the right to pursue the canceled claims in related applications. New claims 83 to 132 have been added, with claims 83 and 108 being the independent claims. New claims 93-96 and 112-115 are withdrawn, but it is respectfully requested that these claims be rejoined and examined should the generic claim be found allowable. These claims are believed to add no new matter to the application. Entry and consideration of the new claims is respectfully requested.

Written support for the claims can be found throughout the specification. For instance, support for claims 83, 84, 86, 88, 91, 93, 95, 97, 107-109, 111, 113, 116, 118, 120, 122, and 132 can be found on page 5, lines 2-8, page 11, line 27 to page 12, line 24, Figure 6, and page 63, line 23 to page 67, line 25. Written support for claims 85, 87, 89, 90, 110, 112, 114, and 115 can be found on page 50, line 16 to page 52, line 7, page 53, line 31 to page 56, line 15, and Figure 2. Exemplary support for claims 92, 94, 96, 98, 117, 119, 121, and 123 can be found on Figure 2, page 53, line 31 to page 56, line 15, and page 6, lines 1-17. Written support for claim 99 and 124 can be found on page 38, lines 25-26. Written support for claims 100-101 and 125-126 can be found on page 5, lines 19-30 and page 34, line 31 to page 35, line 9. Written support for claims 102-103 and 127-128 can be found on page 21, line 24 to page 24, line 2. Written Support for

claims 104-105 and 129-130 can be found on page 20, lines 13-20. Exemplary support for claim 106 and 131 can be found on page 14, lines 19-21.

II. Interview Summary

Applicants would like to thank Examiner Baskar for the courtesy extended during the telephone interview with Applicants' representatives, Elizabeth J. Haanes and Carla Ji Eun Kim on December 20, 2007, and the follow-up conversation with Dr. Haanes on January 10, 2008.

During the interviews, the pending rejections under 35 U.S.C. § 112, first paragraph, a written description rejection and an enablement rejection, were discussed. In addition, the pending art rejections under 35 U.S.C. § 102 (b) were discussed. Finally, based on the Examiner's recommendations, Applicants informed the Examiner that the present reply would be filed.

III. Rejections under 35 U.S.C. §112, First paragraph- Written Description

The Examiner has rejected claims 2, 13, 16, 22, 27-37, 38-48, 49-59, 60-70, 71-72, and 74-82 under 35 U.S.C. § 112, first paragraph, as allegedly "lacking an adequate written description in the specification." Specifically, the Examiner alleges that the instant specification lacks written support for the genus comprising an amino acid sequence at least 95% identical to SEQ ID NO: 2 or at least 95% identical to fragments of SEQ ID NO: 2. In order to expedite the prosecution of this application and not in acquiescence of the Examiner's rejection, Applicants have canceled the previously

pending claims and have submitted new claims 83 to 132. Insofar as the rejection applies to the new claims, Applicants respectfully traverse.

The test for the written description requirement is whether one skilled in the art could reasonably conclude that the inventor had possession of the claimed invention based on the specification as filed. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991); M.P.E.P. § 2163.02. Possession of a claimed genus can be adequately described, *inter alia,* by the "representative number of ***species***" test. *See Regents of the University of California v. Eli Lilly*, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Alternatively, such possession can be shown by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that the applicant was in possession of the claimed genus. *See id.* at 1406; *See also Enzo Biochem Inc. v. Gen Probe Inc.*, 196 F.3d 1316, 1324-25 (Fed. Cir. 2002).

As asserted during the interview on December 20, 2007, Applicants respectfully note that the specification clearly describes a representative number of species. The disclosed genus is an amino acid sequence at least 95% identical to SEQ ID NO: 2, or fragments thereof. The instant specification discloses HMW polypeptide sequences for *C. trachomatis* serovars L2 (SEQ ID NO: 2), B (SEQ ID NO: 15) and F (SEQ ID NO: 16). Figure 6 provides an alignment of the polypeptide sequences for serovars L2, B and F which shows that serovars B and F are about 96% identical to serovar L2. The instant specification also includes an example based on PCR analyses which provides that

highly conserved HMW proteins are also expressed in *C. trachomatis* serovars B, Ba, D, E, F, G, H, I , J, K, L1, L2, and MoPn as well as *C. pneumoniae*. *See* Specification at page 52, line 9 to page 53, line 29.

Furthermore, the specification clearly provides that related HMW proteins can be generated by "one or more amino acid deletions, insertions or substitutions." Specification at page 5, lines 24-25 and page 7, lines 4-23. For instance, as described above, Figure 6 highlights the amino acid residues that are variant between SEQ ID NOs: 2, 15, and 16. There are at least 19 such amino acids residues in the sequence of amino acids 29-533 of SEQ ID NO: 2. A skilled artisan would appreciate that these amino acids could likely be substituted or modified without affecting polypeptide function.

The instant specification also provides that an antibody preparation raised against SEQ ID NO: 2 cross-reacts with SEQ ID NOs: 15 and 16, as well as corresponding polypeptides in *C. trachomatis* serovar MoPn and C. *pneumoniae*, again confirming the preservation of the HMW polypeptide conformation and its function. *See* Specification at page 61, lines 21-33.

Applicants respectfully assert that the specification more than adequately conveys possession of the claimed invention. A skilled artisan would recognize that Applicants were in possession of the entire claimed genus of polypeptides based on the representative number of species disclosed. For all of the above reasons, Applicants assert that the written description requirements have been met and that the Examiner's rejection is overcome. Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

IV. Rejections under 35 U.S.C. §112, First paragraph- Enablement

The Examiner has rejected claims 2, 13, 16, 22, 27-37, 38-48, 49-59, 60-70, 71-72, and 74-82 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. In particular, it is alleged that the instant specification fails to provide enablement for fragments; fails to provide enablement for variants at least 95% identical SEQ ID NO:2 or fragments thereof; and fails to enable an amino acid sequence of SEQ ID NO: 2 wherein said polypeptide is recognizable by an antibody preparation that specifically binds to a polypeptide consisting of the amino acid sequence of SEQ ID NO:2.

In order to expedite the prosecution of this application and not in acquiescence of the Examiner's rejection, Applicants have canceled the previously pending claims and submitted new claims 83 to 132. Insofar as the rejection applies to the new claims, Applicants respectfully traverse.

The test for enablement is whether one of ordinary skill in the art, given the disclosure at the time of filing, could make and use the claimed invention without undue experimentation. *See In re Wands* , 858 F.2d 731, 737 (Fed. Cir. 1988). Several factors must be considered when determining whether experimentation is "undue," including predictability in the art, state of the art, presence or absence of working examples, amount of guidance presented, nature of the invention, breadth of the claims, and level of skill in the art. *Id.* "'The key word is "undue," not "experimentation."' *Id.* at 737 (quoting *In re Angstadt*, 537 F.2d at 504). As provided by MPEP § 2164.01 (Rev. 3, Aug. 2005) at 2100-193, the fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation, as is the

case in vaccine research. In fact, as noted in *Falkner v. Inglis* (quoting the Board) "'the mere fact that the experimentation may have been difficult and time consuming does not mandate a conclusion that such experimentation would have been considered to be 'undue' in this art. Indeed, great expenditures of time and effort were ordinary ***in the field of vaccine preparation***.'" *See Falkner v. Inglis*, 448 F.3d 1357, 1365 (Fed. Cir. 2006)(emphasis added).

The Examiner, referring to the unpredictability of amino acid substitutions or modifications addressed several of the *Wands* factors in the Office Action and alleged that "[t]he specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predictably make or identify the claimed antibodies with a reasonable expectation of success." Office Action at page 7.

Without agreeing to the rejection and for the sole purpose of further expediting prosecution, new independent claims 83 and 108 additionally recite functional characteristics of HMW polypeptides of the invention. Applicants respectfully note that newly submitted claims 83-107 require a pharmaceutical composition comprising the HMW polypeptide or variants thereof to elicit a protective immune response using the well known and accepted mouse genital infectivity model. Likewise, newly submitted claims 108 to 132 require that a pharmaceutical composition comprising the HMW polypeptide or variants thereof, when administered to a subject, induce a cellular immune response or humoral immune response that recognizes the polypeptide of SEQ

ID No: 2. Support for the recited functions can be found throughout the as-filed application, for instance, on page 14, lines 6-19; page 18, lines 23-26 and page 63, line 23 to page 67, line 11. Applicants also respectfully note that co-owned PCT application PCT/US98/20737 (Publication No. WO 99/17741), filed October 1, 1998 and claiming priority to U.S. Patent Application No. 08/942,596 contains corroborating data showing a cellular response and humoral response to a recombinant HMW protein in mice and protection against *C. trachomatis*-induced infertility in female mice challenged with *C. trachomatis* after immunization with a recombinant HMW protein. *See* WO 99/17741 at page 69, line 19 to page 74, line 28.

Applicants respectfully assert that the instant specification enables various fragments of SEQ ID NO: 2, including, but not limited to, amino acids 29-533 and 29-1012 of SEQ ID NO: 2 and polypeptides that are at least 95% identical to these fragments. For example, Example 6 of the instant specification teaches how to make a truncated HMW recombinant protein. Although Example 6 can be used as a template by a skilled artisan to produce any of the recited fragments, the particular HMW protein fragment produced by the cloning described in the example is a polypeptide of amino acids 29-533. *See* Specification at page 40, lines 13-35 and page 50, line 18 to page 52, line 7.

The instant specification also provides general disclosure as to how any of the claimed fragments could be produced using molecular biology techniques known in the art. For instance, page 27, line 25 to page 33, line 5 of the specification describes how one could clone various nucleic acid molecules coding for a HMW polypeptide using the

nucleic acid sequences disclosed. Page 33, line 8 to page 38, line 2 of the specification describes how one could express HMW polypeptides from such cloned sequences. Example 1 on page 39, line 9 to page 40, line 35 describes the isolation and purification of a HMW polypeptide fragment (SEQ ID NO: 3).

Further, the instant specification provides guidance as to how one could go about producing a polypeptide that is at least 95% identical to a peptide fragment of SEQ ID NO: 2. As previously discussed, a skilled artisan could modify amino acids highlighted in Figure 6 as being variant among HMW proteins with the expectation that the modification would most likely not affect the functionality of the polypeptide. Additionally, for example, it would be within the purview of a skilled artisan to substitute an amino acid with another amino acid of the same class of amino acids. For instance, a nonpolar amino acid could be substituted with a different nonpolar amino acid or a basic amino acid could be substituted with a different basic amino acid. *See* Specification at page 6, line 30 to page 7, line 23. Accordingly, Applicants respectfully assert that the instant specification enables the recited fragments of SEQ ID NO: 2 as well as variants of those fragments (*e.g.*, polypeptides at least 95% identical to the fragments).

The claims of the instant application no longer recite an amino acid sequence of SEQ ID NO: 2 wherein said polypeptide is recognizable by an antibody preparation that specifically binds to a polypeptide consisting of the amino acid sequence of SEQ ID NO:2. Regardless, Applicants respectfully assert that the instant specification enables

the preparation and use of such an antibody. The Examiner is respectfully directed to page 61, line 2 to page 64, line 23 of the instant specification.

Accordingly, Applicants respectfully request that the enablement rejection under 35 U.S.C. §112, first paragraph, be withdrawn.

V. Rejections under 35 U.S.C. §102(b)

The Examiner has rejected claims 2, 21, 27, 28, 31, 32, 37, 38, 42-43, 48, 49, 50, 53, 54, 59, 60, 61, 64, 65, 70, 71-73, 76, and 82 under 35 U.S.C. §102(b) as being anticipated by Caldwell *et al.*, *Infec. and Immun.*, 31(3):1161-76 (1981) ("Caldwell") as evidenced by Mygind *et al.*, *FEMS Microbiol. Lttrs*, 186:163-169 (2000) ("Mygind"). The Examiner alleges that Caldwell "substantially purified" a 105-109kDa polypeptide in Figure 2. *See* Office Action at page 4. The Examiner further alleges that "the protein and fragments (peptides) are substantially purified by SDS PAGE." *Id.* (citation omitted).

While not in acquiescence with the Examiner's rejection, but to facilitate the prosecution of this application, all previously pending claims have been canceled, rendering rejection of these claims moot. Insofar as this rejection applies to newly-added claims 83-132, Applicants respectfully traverse.

Anticipation requires that all the elements and limitations of the claims are found, either explicitly or inherently, within a single reference. There must be no difference between the claimed invention and the reference disclosure as viewed by one of ordinary skill in the art. *Scripps Clinic & Research Fdn. v. Genentech*, 927 F.2d 1565, 1576 (Fed. Cir. 1991). Absence from a cited reference of any element of a claim negates anticipation of that claim by that reference. *Atlas Powder Co. v. E.I. Dupont de Nemours*

& Co., 224 U.S.P.Q. 409 (Fed. Cir. 1984). In the event that a reference does not explicitly teach all elements of a claim, anticipation can be shown by inherency if, and only if, the cited reference makes clear that the missing descriptive matter is *necessarily present* in the thing described in the reference. *Continental Can Co. USA Inc. v. Monsanto Co.*, 948 F.2d 1264 (Fed. Cir. 1991). Inherency may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. *In re Oelrich*, 212 U.S.P.Q. 323, 326 (C.C.P.A. 1981).

The newly added claims are directed to a pharmaceutical composition comprising an isolated polypeptide at least 95% identical to amino acids 29-533 of SEQ ID NO: 2, wherein said composition eliminates or reduces the level of *C. trachomatis* in the lower genital tract following intravaginal challenge when administered to female mice, or wherein the claimed HMW polypeptide, when administered to a subject, induces a cellular immune response or humoral immune response that recognizes the polypeptide of SEQ ID No: 2. Caldwell does not anticipate the pharmaceutical composition claims because it does not teach all the limitations of the claims and does not enable a person of ordinary skill to carry out the invention.

A. CALDWELL DOES NOT TEACH AN "ISOLATED" POLYPEPTIDE.

The Examiner alleges that Caldwell "substantially purified" the proteins with molecular weight of approximately 105-109kDa shown in Figure 2. *See* Office Action at page 4. The Examiner further alleges that "Caldwell discloses high molecular weight protein 105-115 kD but fails to note the inherent property of the amino acid sequence of an isolated polypeptide comprising SEQ ID NO: 2 ... or amino acids 29-533 of SEQ ID

NO: 2 ... [amino acids] 29-1012 of SEQ ID NO: 2." *Id.* at page 8. From this, it appears that the Examiner alleges that an impure protein mixture inherently anticipates an isolated polypeptide. The Examiner's conclusion is based on the fact that the isolated polypeptide would be inherently present in the impure mixture even though the polypeptide was not known prior to the invention. Applicants respectfully traverse.

Courts have firmly established early in 1970s the legal principle on anticipation of an "isolated" substance, *e.g.*, a polypeptide by an unidentified mixture of substances. In particular, *In re Kratz* established that a substantially purified compound is not anticipated by a naturally occurring material inherently containing the compound. 592 F.2d 1169, 1174 (C.C.P.A 1979). In *Kratz*, the claims on appeal were directed, *inter alia*, to compositions comprising "substantially pure 2-methyl-2-pentenoic acid" ("2M2PA"), a substance used to impart strawberry flavor to foods. The compositions were rejected as being obvious over the Mussinan reference (among others) which disclosed:

> methods used to extract "volatile acids" from fresh strawberries. The thus-extracted acids (including 2M2PA) were analyzed on a mass spectrometer after separation via a gas chromatograph. Of the 33 acids identified, 22 are being reported for the first times as constituents of strawberry.

Id. at 1171. The claimed substance, 2-methyl-2-pentenoic acid, was one of the substances 33 identified by mass spectroscopy. The CCPA reversed, noting that:

> [a]ppellants do not seek to claim 2M2PA, per se, nor 2M2PA in its natural state, nor even a composition encompassing strawberries; but instead present claims to compositions containing "substantially pure" 2M2PA and preparative methods thereof. Since the claims do not encompass

> natural compositions, in that "substantially pure" 2M2PA does not apparently occur in nature, one portion of the test is not met.
> *Id.* at 1174.

The C.C.P.A. in *In re Bergstrom* further clarified and expanded that an isolated polypeptide is "new" and thus patentable over a polypeptide mixture. *In re Bergstrom*, 57 F.2d 1394, 1401-1402 (C.C.P.A. 1970). In *Bergstrom*, the claims were directed to purified prostaglandin E2 ("PGE(2)") and prostaglandin E3 ("PGE(3)"). *Id.* at 1395. The examiner in *Bergstrom* rejected the claims for not being 'new,' alleging that PGE(2) and PGE(3) were inherently present in the mixture described in Bergstrom *et al.*, *Acta Chemica Scandinavica* 14: 1693-1705 (1960) ("the 1960 article"). *Bergstrom* at 1395-1398. The 1960 article disclosed isolation from prostate gland of PGE(1), which displayed both a smooth muscle stimulating and hypotensive activity. *Id.* at 1395-1398. In the process of isolating PGE(1), the 1960 article disclosed, as an intermediate purification step, elution of PGE(1) in a fraction which was subsequently shown to be a mixture of PGE(1), PGE(2) and PGE(3). But at the time, the other elements in the mixture were not known. The patent applicants in *Bergstrom* performed the same purification steps as the 1960 article up to and including this elution step. The applicants then performed further isolation steps on the three-component mixture to isolate PGE(2) and PGE(3). *Id.*

In response to the rejection, the applicants in *Bergstrom* argued that the PGE(2) and PGE(3) were "isolated" relative to the mixture taught in the 1960 article. *Id.* at 1401. Furthermore, the applicants pointed out that "the art knew nothing of the existence of PGE(2) and PGE(3) prior to their isolation of them," and thus no one knew that PGE(2) and PGE(3) could be isolated from the mixture disclosed in the 1960 article. *Id.* at 1400.

The facts set forth in *Bergstrom* are very similar to the facts of the present application. In *Bergstrom*, the 1960 article inherently contained the claimed prostaglandins in the mixture. Here, Caldwell may inherently contain the claimed polypeptide in the gel. In *Bergstrom*, the existence of the two additional prostaglandins was not known. Here, the existence of the claimed HMW polypeptide, or any specific high molecular weight polypeptide, contained in the band, was not known. In both *Bergstrom* and here, the examiners rejected the pending claims, alleging that the claimed substance was inherently present in the reference. Most importantly, in *Bergstrom*, the 1960 article separated the mixture to a certain degree, *i.e.*, a mixture of three substances. Here, it can now be shown that Caldwell separated a much cruder mixture than the 1960 prostaglandin article.

The Caldwell gel band at "105kDa" represents a much cruder preparation than the 1960 article in *Bergstrom* because, *inter alia*, the acrylamide gels used in Caldwell were not appropriate to separate out high molecular weight proteins. High molecular weight proteins are difficult to resolve and even more difficult to size in high percentage acrylamide gels such as a constant porosity 12.5% acrylamide gel due to the small pore size. A 12.5% acrylamide gel, as used in Caldwell, is suitable to separate only 10-70 kDa proteins. Under these electrophoresis conditions, high molecular weight proteins tend to migrate slower in the imposed electric field and "clump" together. As such, proteins larger than 70kDa are retarded in their migration through the gel, and thus aggregate together at the top of the gel. *See Gel Electrophoresis of Proteins A Practical Approach*. Hames, B.D. and Rickwood, D. ed, IRL Press Ltd, Oxford. (1981) (relevant portions attached hereto as Exhibit 1, *see*, in particular, the figure on p. 16). In fact, the

high molecular weight protein "clump" would have contained up to 14 or more unidentified *C. trachomatis* proteins having a molecular weight greater than about 70kDa migrating together. *See* http://www.gram.au.dk/CTRtable.html (last visited February 11, 2008, attached hereto as Exhibit 2).

Upon the facts set forth in *Bergstrom*, the *Bergstrom* court held that "by definition, pure materials necessarily differ from less pure or impure materials and, if the latter are the only ones existing and available as a standard of reference, as seems to be the situation here, [] the 'pure' materials are 'new' with respect to them." *Id.* at 1402. Similarly, the claimed *isolated* HMW polypeptide is not anticipated by Caldwell. According to *Bergstrom*, the claimed *isolated* HMW polypeptide necessarily differs from the crude mixture of the 14 proteins in Caldwell. The claimed *isolated* HMW polypeptide was new at the time the application was filed. Therefore, even assuming, *arguendo*, that Caldwell's protein mixture was "isolated" to a certain degree, so too were PGE(2) and PGE(3) "purified" to a certain degree. Accordingly, the *isolated* HMW polypeptide is 'new' with respect to the 'less isolated,' or rather crude, protein mixture in Caldwell.

Based on the facts and the Court's holding in *Bergstrom*, Applicants argue that the Examiner's rejection is clearly contrary to the well and long settled legal principle of anticipation decided in *In re Kratz* as well as *Bergstrom*. Accordingly, Applicants respectfully request that the rejection be withdrawn.

B. CALDWELL FAILS TO ENABLE THE CLAIMED COMPOSITION.

Applicants also respectfully assert that Caldwell fails to enable the claimed pharmaceutical composition. Anticipation requires a prior art reference to be enabling such that the claimed subject matter may be made or used by one skilled in the art. *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1354 (Fed. Cir. 2003). A reference is enabling if it teaches those of ordinary skill in the art enough that they can carry out the invention without "undue experimentation." *Elan Pharmaceuticals, Inc. v. Mayo Foundation,* 346 F. 3d 1051, 1057 (Fed. Cir. 2003). While proof of efficacy is not required for a reference to be anticipatory, if a reference discloses a genus of elements, a person of ordinary skill in the art must be able to immediately envisage a particular species element for that species to be enabled. *See, e.g., In re Petering*, 301 F.2d 676, 681 (C.C.P.A. 1962) (distinguishing a broad genus of chemical compounds (species not enabled) from a subgenus of approximately 20 readily-envisionable species (each species therein enabled)).

Caldwell does not enable a person of ordinary skill in the art to make the isolated polypeptide or the claimed composition. First, as clearly evidenced by Mygind, in view of Caldwell, a person of ordinary skill in the art could not possibly carry out the present invention without undue experimentation. Second, Caldwell shows, at most, a mixture of unidentified higher molecular weight polypeptides on a gel. Since its existence was unknown, the "species" of the present invention, *i.e.*, the isolated HMW polypeptide or pharmaceutical composition comprising the HMW polypeptide, could not possibly have been envisioned, and therefore Caldwell cannot be enabling.

The Examiner has cited Mygind as evidence that the claimed isolated polypeptide was allegedly present in gel band shown in Figure 2A of Caldwell. However, the extensive efforts which were required for Mygind to finally "isolate" the pmpG polypeptide described therein, a full 19 years after the publication of Caldwell, clearly demonstrates that undue experimentation was required. Prior to the Mygind publication (but subsequent to the filing of present application), the genomes of two *Chlamydia* species, *C. pneumoniae* and *C. trachomatis* serotype D were completely sequenced, and encoded polypeptides were deduced. These sequences were relied upon heavily to predict the existence of pmp proteins in *C. trachomatis* serotype L_2. For example, Mygind notes that "[a]mong the *most interesting discoveries* [in the sequence analyses] was the existence of a larger group of potential outer membrane proteins (Pmp)." Mygind at p. 163 (emphasis added).

Even given the heavy reliance on the previously sequenced *Chlamydia* genomes, extensive further experimentation was required to "isolate" PmpG (the claimed isolated HMW polypeptide). As shown in Figure 2B (*Id.* at p. 165), in order to "isolate" PmpG from other *Chlamydia* polypeptides, Mygind describes at least eight additional steps which were required to finally identify and isolate PmpG. Clearly, starting with the disclosure in Caldwell, for a protein chemist, the experimentation required to "isolate" PmpG as presently claimed was "undue." Accordingly, Applications respectfully assert that Caldwell not only fails to teach, but also fails to enable the claimed HMW polypeptide of the instant application.

Furthermore, a person of ordinary skill in the art would understand that a high molecular weight protein band of a whole cell bacterial lysate visible on a 12.5% polyacrylamide gel or exposed on an auto-radiograph, as provided in Caldwell, would contain a large mixture of unidentified proteins having a broad range of molecular weights. Since no specific isolated polypeptide could have been envisaged in such a mixture, the Caldwell reference does not enable the isolated HMW polypeptide, let alone the claimed pharmaceutical composition comprising the polypeptide, and therefore cannot anticipate it.

C. CALDWELL DOES NOT TEACH A PHARMACEUTICAL COMPOSITION.

Applicants further note that all currently pending claims recite a pharmaceutical composition comprising an isolated HMW polypeptide. Because Caldwell does not teach an isolated HMW polypeptide, the reference also does not teach a pharmaceutical composition comprising such a polypeptide and a carrier.

Based on the above remarks, Applicants respectfully point out to the Examiner that Caldwell does not anticipate the claimed invention, and request that the rejections to the claims under 35 U.S.C. § 102(b) be withdrawn.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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